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10/580,306	09/26/2006	Andrew Simon Bell	PC25572A	5713

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EXAMINER	
MOORE, SUSANNA	
ART UNIT	**PAPER NUMBER**
1624	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,306	BELL ET AL.	
	Examiner	Art Unit	
	SUSANNA MOORE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 11/10/2008 is acknowledged. Group I, drawn to pyrazolo[4,3-d]pyrimdines and simple compositions thereof, embraced by claims 1-14 was elected by Applicant. Applicant has not pointed to any errors in the Examiners analysis of the classification of the different inventions. The requirement is deemed proper and is therefore made **FINAL**.

There are nineteen claims pending and nineteen under consideration. Claims 1-12 and 14 are compound claims. Claim 13 is a composition claim. Claim 15 is drawn to nonelected subject matter. This is the first action on the merits. The application concerns some pyrazolo[4,3-d]pyrimidine compounds, compositions, synthesis, and uses thereof.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Substituted Pyrazolo[4,3-d]pyrmidines as Phosphodiesterase Type 5 (PDE-5) Inhibitors.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/31/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

Claim 14 is objected to because of the following informalities: claim 14 is drawn to a compound claim with intended uses. The intended use is not given patentable weight. Note *In re Tuominen* 213 USPQ 89. Applicant should cancel claim 14 since the removal of the intended use does not further limit claim 1. Appropriate correction is required.

Claims 5-9, 13 and 14 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n).

Claim 14 is objected to because of the following informalities: the phrase, "congestive heart failure" is repeated in said claim. Appropriate correction is required.

This application contains claim 15, drawn to an invention nonelected without traverse in the paper of 11/10/2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites the limitation "tetrahydropyranyl" in the definition of R^5. There is insufficient antecedent basis for this limitation in the claim.

Claims 1-11, 13 and 14 are vague. The terms, "such as," "particularly," and "includes" are open-ended. What is excluded? Thus the metes and bounds of said claims cannot be ascertained. See claim 1, page 133, lines 4, 14 and 16; claim 8, lines 5, 12 and 14; and claim 14, lines 4, 7, 8, 10, 17 and 19.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compound of claim 1 or pharmaceutically acceptable salts of said compound does not reasonably provide enablement for a solvate of a compound of claim 1. The specification does not provide sufficient guidance nor does it enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention is a compound of claim 1, or a pharmaceutically acceptable salt of said compound. There is a **general** teaching of solvates or polymorphs of compound of claim 1 in the Specification on pages 24-25.

The state of the prior art and predictability or lack thereof in the art

It is the state of the prior art that the term "solvate" found in the claims is defined as a compound formed by solvation (the combination of solvent molecules with molecules or ions of the solute. It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. Predicting the formation of solvates or polymorphs of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or polymorphs and hence generalizations cannot be made for a series of related compound (See Vippagunta, et al. and Thayer et. al.)

The scope of "solvate or polymorph" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active in vivo. Solvates or polymorphs can not be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular solvate or polymorph.

The amount of direction or guidance present and the presence or absence of working examples

There is no direction or guidance present in the specification or working examples present in the specification are that defines or relates to what solvates are being included in the elected invention.

The breadth of the claims

The breadth of the claims is a compound of claim 1 or a pharmaceutically acceptable salt or solvate o rpolymorph thereof.

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to prepare compounds with various solvents without any direction as to what compounds form solvates with which solvents.

The level of skill in the art is high without showing or guidance as to how to make solvates of a conjugate of claim 1 it would require undue experimentation to figure out the

solvents, temperatures and reaction times that would provide solvates or polymorphs of the above compounds.

To overcome this rejection, Applicant should submit an amendment deleting the term "solvate or polymorph" or provide evidentiary support for solvate or polymorph.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims.

(a) Scope of the compounds. The instant claims encompass millions of compounds with

a pyrazolo[4,3-d]pyrimidine scaffold with a variety of substituents at six different positions.

(b) Scope of the diseases covered. Claim 14 is drawn to an intended use of compounds of formula (I), for hypertension (including essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension), angina (including stable, unstable and variant (Prinzmetal) angina), stroke, coronary artery disease, congestive heart failure, conditions of reduced blood vessel patency (such as post-percutaneous coronary angioplasty), peripheral vascular disease, atherosclerosis, nitrate-induced tolerance, nitrate tolerance, diabetes, impaired glucose tolerance, metabolic syndrome, obesity, sexual dysfunction (including male erectile disorder, impotence, female sexual arousal disorder, clitoral dysfunction, female hypoactive sexual desire disorder, female sexual pain disorder, female sexual orgasmic dysfunction and sexual dysfunction due to spinal cord injury), premature labour, pre-eclampsia, clysmenorrhea, polycystic ovary syndrome, benign ,prostatic hyperplasia, bladder outlet obstruction, incontinence, chronic obstructive pulmonary disease, acute respiratory failure, bronchitis, chronic asthma, allergic asthma, allergic rhinitis, gut motility disorders (including irritable bowel syndrome), Kawasaki's syndrome, multiple sclerosis, Alzheimer's disease, psoriasis, skin necrosis, scarring, fibrosis, pain (particularly neuropathic pain), cancer, metastasis, baldness, nutcracker oesophagus, anal fissure and haemorrhoids.

Several of the "umbrella" terms will be discussed below.

Chronic Obstructive Pulmonary Disease (COPD) is a slowly progressive disease of the airways that is characterized by a gradual loss of lung function. COPD includes chronic obstructive Bronchitis (which involves inflammation and eventual scarring of the bronchi) and

emphysema (enlargement and destruction of the alveoli). Emphysema comes in several forms, including Congenital Lobar Emphysema, Bullous Emphysema, Centrilobular Emphysema (Proximal acinar emphysema), Panacinar (panlobular), Distal acinar (paraseptal) as well as Alpha-1 antitrypsin (AAT) deficiency, which is the genetic form of emphysema; patients often have both a form of bronchitis and emphysema. Ordinary chronic bronchitis is sometimes included with COPD even if there is no actual obstruction, and asthmatic bronchitis is generally included in COPD as well. Persons with COPD typically develop smaller air passageways, which can become clogged with mucus and have partially destroyed alveoli. There is no pharmaceutical treatment for COPD per se. Instead, treatment is supportive and designed to relieve symptoms and improve quality of life. Thus, oxygen is often given to partially compensate for the loss of lung function. Bronchodilators can expand passageways in the lungs, Corticosteroids can reduce inflammation and Antibiotics can ward off bacterial infections, but none of these treat the COPD itself.

The compounds are claimed as particularly useful for the treatment of cancer including solid tumors such as skin, breast, brain, cervical carcinomas, testicular carcinomas, etc. More particularly, cancers that may be treated by the compounds, compositions and methods of the invention include, but are not limited to: Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma,

leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Karposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney (adenoearcinoma, Wilm's tumor [nephroblastoma], lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple mycloma, malignant giant cell tumor chordoma, osteochronfroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma [pinealoma], glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological:, uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma [serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma], granulosa-thecal cell tumors, Sertoli- . Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma,

intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia [acute and chronic], acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma [malignant lymphoma]; Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Karposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids; and Adrenal glands: neuroblastoma. Thus, the term "cancerous cell" as provided herein, includes a cell afflicted by any one of the above identified conditions.

Benign tumors include, but are not limited to: squamous cell papilloma, basal cell tumor, transitional cell papilloma , adenoma, gastrinoma, cholangiocellular adenoma, hepatomo cellular adenoma, renal tubular adenoma, glomus tumor, fibroma, myxoma, lipoma, leiomyoma, rhabdomyoma, benign teratoma, hemangioma, lymphangioma, osteoma, chondroma and meningioma.

Heart disease is one of a number of different diseases which afflict the heart. The most common heart diseases are:

- heart disease, the end result of the accumulation of atheromatous plaques within the walls of the arteries that supply the myocardium
- Ischaemic heart disease, a disease characterized by reduced blood supply to the heart.
- Cardiovascular disease, a class of diseases that involve the heart and/or blood vessels (arteries and veins).Implies under this category some popular diseases like: diabetes, high blood pressure and hypercholesterolemia.
- Pulmonary heart disease, a failure of the right side of the heart.

- Hereditary heart disease
- Hypertensive heart disease
- Inflammatory heart
- valvular heart disease

Functional gut motility disorders can be defined as any disease or disorder associated with the GI tract, which include the mouth, esophagus, stomach, intestines, rectum and anus. Other organs, such as the spleen, bile ducts, gall bladder, liver and pancreas, can also be a cause of gastrointestinal disorders. As recited, the scope of the claim can include, but is not limited to, tooth decay, periodontal disease, abscesses, canker sores, cold sores, oral cancer, gastroesophageal reflux disease, dysphagia, esophagus cancer, circopharyngeal incoordination, achalasia, diverticula, burning mouth syndrome, pancreas cancer, Crohn's disease, colon polyps, diverticular disease, intestinal parasites, salivary gland disease, sialhorria, dentigerous cyst, glossitis, benign migratory, Ludwig's Angina, Melkerson-Rosenthal Syndrome, xerostamia, Pierre-Robin Syndrome, diabetes, lactose intolerance, bruxism,ulcerative colitis, cystic fibrosis, pernicious anemia, tropical sprue, cirrhosis, Bassen-Kornzweig syndrome, pancreatitis, Shwachman-Diamond syndrome, anal cancer, acute pancreatitis, anal fissure, anal fistula, colorectal cancer, hemorrhoids, perirectal abscess, proctitis, rectal prolapse, functional constipation, liver cancer, diarrhea, ankyloglossia, Irritable Bowel Syndrome, functional dyspepsia, peptic ulcer, intussusception, Coeliac disease, Whipple's disease, lymphoma, incontinence, chronic pancreatitis, Hirschsprung's disease, infant regurgitation, biliary disorder, hemochromatosis, Wilson disease, tyrosinemia, alpha 1 antitrypsin defiency, glycogen storage disease, primary sclerosing cholangitis, hepatitis A, hepatitis B, hepatitis C, Reyes's syndrome.

These are just a few of the diseases covered by the scope of claim 14.

(B) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) Direction or Guidance: That provided is very limited. The dosage range information is provided on page 39 of the Specification, 0.01 mg/kg - 50 mg/kg. Moreover, this is generic, the same for the many disorders covered by the Specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for the diseases covered by the Scope of diseases above.

(D) State of the Prior Art: These compounds are substituted pyrazolopyrimidine compounds. Sildenafil, Tadalafil and Vardenafil are selective inhibitors of type V phosphodiesterase (PDE V) and are used as remedies for erectile dysfunction. The state of the prior art in PDE 5 diseases is provided by Perry (Current Opinion in Chemical Biology). Perry states in the first sentence, first complete paragraph, column 2, page 478 that "the role of PDE5 inhibitors in cardiovascular therapy has yet to be clinically established". He reports that the FDA has approved the PDE 5 inhibitor Viagra (sildenafil) only for the treatment of "male impotence and erectile dysfunction". Corbin (Int J Clin Pract.) states "inhibitors that are selective for phosphodiesterase- 5 (PDE5)

represent a promising new class of compounds that are useful for the treatment of erectile dysfunction and perhaps other disorders". "[P]erhaps" is not the standard for disease treatment enablement. Cremers (Herz) states in his abstract, "little is known about other potential beneficial effects of [the PDE 5 inhibitor] sildenafil". "[S]ildenafil may be a useful adjunct to inhaled iloprost in the management of pulmonary hypertension." "In gastrointestinal disorders, sildenafil also exerts several effects which might be of clinical relevance." Thus, in 2003, applications of sildenafil to treatment of diseases other than erectile dysfunction were speculative.

(E) Working Examples: There is an in vitro assay, drawn to inhibition of the enzyme PDE-5 described in the passage spanning pages 128-130 with data on 10 compounds. Applicants do not state and it is not recognized in the arts this assay is correlated to clinical efficacy for the treatment of any human diseases besides erectile dysfunction.

(F) Skill of those in the art: This involves physiological activity. The nature of the invention requires an understanding of the PDE-5 as well as the factors leading to its inhibition. **The instant case is enabled for treating erectile dysfunction**, but is not enabled for treating every disease covered by claim 14.

There is no pharmaceutical treatment for COPD per se. Instead, treatment is supportive and designed to relieve symptoms and improve quality of life. Thus, oxygen is often given to partially compensate for the loss of lung function. Bronchodilators can expand passageways in the lungs, Corticosteroids can reduce inflammation and Antibiotics can ward off bacterial infections, but none of these treat the COPD itself.

Currently, there is no treatment for Alzheimer's disease, per se. Currently the only medications offer relatively small symptomatic benefit for some patients but do not slow disease progression. For example, acetylcholinesterase inhibitors, (Aricept®, Cognex®, Exelon®, and Reminyl®), and voltage-dependent NMDA-antagonists, (Memantine), are the only two chemical treatments available, which have properties these compounds are not disclosed to have. Indeed, p-38 is not currently even considered an important research area, and thus the skill level in the art of p-38 treatment for Alzheimer's disease is especially low. The Palmer TRENDS in Pharmacological Sciences 23(9) 426-433 September 2002 article on drug therapy for Alzheimer's Disease is likewise mentioned; it too makes no mention of p-38.

One of ordinary skill in the art knows that no organic cause has ever been found for irritable bowel syndrome (IBS). There are at present no pharmaceutical treatments for IBS itself, just general medicines such as laxatives or tranquilizers for relief of symptoms. The reference Jones et al, "British Society of Gastroenterology guidelines for the management of the irritable bowel syndrome." Gut 2000, (Suppl II)47:ii1-ii19 makes it clear that no pharmaceutical agent has been established as effective against this serious disorder.

These diseases and disorders covered by the Scope of diseases above cannot be treated generally by any one drug. These are all different diseases and disorders, which occur at different locations and by different modes of action in the body.

Furthermore, currently there is no actual treatment for multiple sclerosis itself, only management of symptoms.

(G) The quantity of experimentation needed: Owing especially to factors A, D, E and F, the

amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Double Patenting

No obviousness-type double patenting rejections over co-pending applications 12112681, 11913091, 10599702, 10997191, 11831021, 10834484 are being made because there is no overlap at R^5. Thus, the obviousness-type double patenting was considered but not applied. The structural difference between the species of the instant Application and co-pending applications 12112681, 11913091, 10599702, 10997191, 11831021, 10834484 means that they are patentably distinct.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624